

TOPOLOGICAL CHIRALITY OF CERTAIN MOLECULES

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§1. INTRODUCTION

MOTIVATED by a combination of intellectual curiosity, aesthetics, and hopes of discovering compounds with novel properties, chemists have been trying for some time to find, in particular to synthesize, molecules with topologically interesting structures. According to [3], the idea of molecules made of linked rings as a realistic possibility was discussed at least as early as 1912. This was about 50 years after the ideas of atomic connectivity and molecular graphs began to be developed. About 50 years still later, E. Wasserman announced [11] the synthesis of a few milligrams of an oil he called a “34,34 catenane”, a substance whose molecular graph would be two closed hydrocarbon rings (each of length 34, one having two oxygen atoms attached) linking each other once. Wasserman’s approach was statistical: make lots of linear molecules bite their own tails and be able to isolate the relatively small number (see [3] for a discussion of probabilities) of linked pairs.

Meanwhile, other groups of chemists, e.g. Schill *et al.*, were pursuing the alternative approach of “directed synthesis”, where the route of synthesis itself is the main proof of structure for the final product (see [6], esp. Ch. 9, for abundant detail) and they too obtained catenanes. It is characteristic of this kind of approach that rigid geometry in a “precatenane” such as shown in Fig. 1(a) guarantees that predictable parts of the molecule are above or below the plane of another part, which in turn leads eventually to the formation of linked rings (Fig. 1(b)) where topology rather than rigid geometry is responsible for the connection of the two rings.

The approach used in [10] to synthesize a “molecular Möbius band” was partly statistical, mostly controlled. A molecule shaped like a ladder with three rungs (Fig. 2) was made to join itself end-to-end. Models and other steric considerations suggested that sometimes the joining would involve one half-twist. Two products were isolated: a solid shown to have molecular graph schematically represented as Fig. 2(a) and an oil which all data indicates is a racemic mixture of left- and right-handed Möbius ladders (b).

There has been frequent speculation on the synthesis of knots “from scratch”, and D. Walba ([8] + conversations) may in fact have achieved them. Since the early 1960’s, many

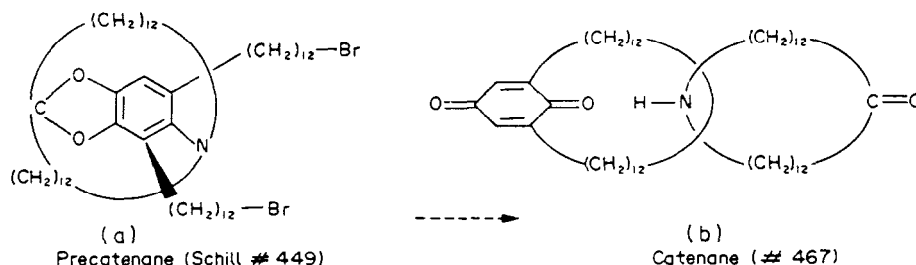


Fig. 1.

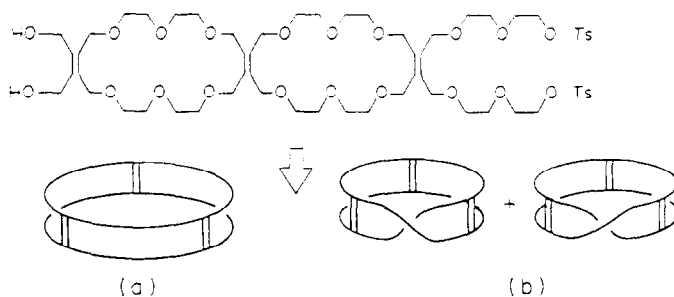


Fig. 2. Molecular Möbius strip.

papers have been published discussing cyclic single- and double-stranded DNA, and the phenomenon of linked rings has become a basic part of our understanding. Besides the intimate linking of parallel strands, DNA molecules are so large (e.g. 5–10,000 nucleotides, 30–60,000 atoms) that electron microscope pictures actually show knots and links. This might seem just the accidental behavior of long, irregular closed curves; however, using recombinant DNA techniques and taking of advantage of some geometric rigidity, direct synthesis of knots and links has been reported. (See [9, Part VI] for discussion of this and other aspects of DNA geometry vs topology.)

The review articles [7] and [9] provide numerous other examples of molecules that have been synthesized with topologically (and/or geometrically) interesting structures.

To interpret the NMR and other data gathered to establish the structure of a particular molecule one needs to consider the symmetries that a proposed structure might exhibit (under appropriate conditions, e.g. certain temperature range). The molecule is assumed to be moving rapidly between its various allowable configurations, rendering certain of its constituent atoms indistinguishable. Smaller organic molecules have usually been viewed as rigid, or as made of rigid parts attached by swivels, and so the allowable symmetries would be primarily a matter of rigid geometry. But to understand the behavior of larger molecules, e.g. the catenanes and Möbius band illustrated above, it seems reasonable to treat the structures as flexible. For example, it is necessary [8] to postulate that the allowable symmetries of the Möbius molecule include non-rigid motions in order to account for the NMR spectroscopy data.

It thus becomes a problem of legitimate interest to chemists to determine the *topological symmetries* of a given molecule: Abstract the molecule as a graph in space (with possibly several different types of vertices, several different types of edges, and perhaps also attached 2- or 3-cells representing aromatic systems) and determine which automorphisms of the graph can be realized by ambient isotopy. A related problem is that of *topological equivalence*: given two embeddings of the graph in space, determine whether or not they are ambient isotopic; in particular, decide if a molecule is *topologically chiral*, that is ambient isotopic to its mirror image. As purely mathematical problems, these are a natural continuation of classical knot theory.

As problems in chemistry, the two above are asking for theoretical limits on the symmetries and equivalences a molecular structure actually can exhibit. According to [10], the Möbius ladder M_3 (see Section II below) with rungs distinguished from edges has the dihedral group D_6 as its non-rigid molecular symmetry group. In the proof of Theorem II.1 below, the first paragraph can be reinterpreted as saying that all automorphisms of the graph M_3 (with rungs vs edges) can be realized within this group; so this is a case where the theoretical upper bound is achieved. The chemical evidence is [8] that M_3 (as well as the other

Möbius molecules M_n does not interconvert with its mirror image. In [8] and [9] the analogous topological conjecture is made: that the embedding of the graph M_n shown in Fig. 3 (with vertical edges colored differently from the rest in the case $n = 3$) is not ambient isotopic to its mirror image; this is established in Theorem II.1 and Corollary II.2. The graph M_3 is isomorphic to the bipartite graph $K_{3,3}$ which is one of the two basic nonplanar graphs of Kuratowski. The other, K_5 , also has been realized chemically and it is conjectured in [9] that this too is topologically chiral. In Section III, the methods of Section II are used to establish the topological chirality of the Simmons–Paquette K_5 molecule.

§II. TOPOLOGICAL CHIRALITY OF MÖBIUS LADDERS

In this section we show that the graphs M_n ($n \geq 3$) (Fig. 3) are not ambient isotopic to their mirror images M_n^* . In the case where $n = 3$, we need to insist that the “sides” of the ladders can be distinguished from the “rungs”; for the cases $n \geq 4$, Corollary II.2, we need no such assumption since any automorphism of a graph M_n ($n \geq 4$) leaves the cycle $a_1 a_2 \dots a_n a_1' \dots a_n' a_1$ invariant (Lemma II.2.1). In any case, the molecules described in Section I above do have distinguished “sides” vs “rungs”. In Fig. 4 we illustrate an isotopy between (graphs easily seen to be isotopic to) M_3 and M_3^* , which indicates the need for the sides vs rungs hypothesis in Theorem II.2. Incidentally, if we ignore the edges $a_3 a_3'$ and $b_3 b_3'$ in Fig. 4 it is easy to see an isotopy of S^3 taking M_2 to M_2^* that translates the circle $a_1 a_2 a_1' a_2' a_1$ rigidly to $b_1 b_2 b_1' b_2' b_1$.

THEOREM II.1. *There exists no isotopy of the 3-sphere S^3 taking the graph M_3 to its mirror image M_3^* in such a way that the set of (unoriented) edges $\{a_k a_k'\}_{k=1,2,3}$ is identified with $\{b_j b_j'\}_{j=1,2,3}$.*

Proof. Suppose such an isotopy exists, and let $h: S^3 \rightarrow S^3$ be the orientation preserving space homeomorphism induced. Since h maps the edges $\{a_k a_k'\}$ to the edges $\{b_j b_j'\}$, h must map the cycle $C = a_1 a_2 a_3 a_1' a_2' a_3' a_1$ to some cyclic permutation of the corresponding cycle $C^* = b_1 b_2 b_3 b_1' b_2' b_3' b_1$ or its inverse. If we deform M_3^* to the symmetric form of Fig. 5 it is easy to see ambient isotopies that move C^* ahead one “click” (move the apparent Möbius band within itself so its center circle rotates 120°) or that reverse the orientation of C^* (rotate 180° about the axis $b_3 b_3'$). Thus, by following h with an additional isotopy if necessary, we may assume that h maps the vertices a_1, a_2, \dots to b_1, b_2, \dots respectively.

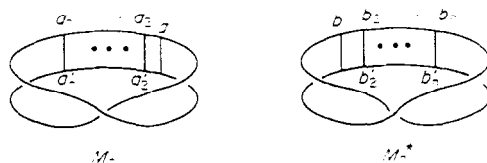


Fig. 3. Möbius ladders.

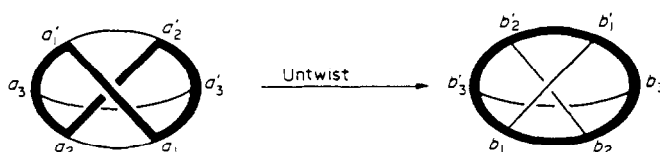
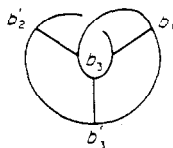


Fig. 4. Isotopy of M_3 to M_3^* .

Fig. 5. The graph M_3^* .

Since h maps the curve C to C^* , h induces [2] an orientation preserving homeomorphism \tilde{h} of the 2-fold cyclic branched cover of S^3 branched along C to the 2-fold cyclic branched cover of S^3 branched along C^* . Since C and C^* are unknotted curves, the branched coverings of S^3 are just S^3 again. Since \tilde{h} covers h , \tilde{h} must map the lift of M_3 to the lift of M_3^* and respect the vertex numbering. If we view the graphs as in Fig. 4 we see that the lifts \tilde{M}_3 and \tilde{M}_3^* are as shown in Fig. 6.

Each of the arcs $a_k a_k'$ (resp. $b_k b_k'$) lifts to a simple closed curve which we call α_k (resp. β_k). Our original problem now translates into showing that there is no orientation preserving homeomorphism \tilde{h} of S^3 taking the link $\alpha_1 \cup \alpha_2 \cup \alpha_3$ to its mirror image $\beta_1 \cup \beta_2 \cup \beta_3$.

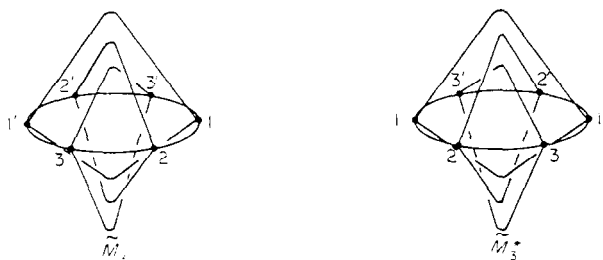
Choose either orientation for α_1 (resp. β_1) and orient α_2, α_3 (resp. β_2, β_3) so they each have linking number $+1$ with α_1 (resp. β_1). Note, from Fig. 6, that with such orientations, the linking numbers $\text{Lk}(\alpha_2, \alpha_3) = +1$ and $\text{Lk}(\beta_2, \beta_3) = -1$. Since \tilde{h} respects vertex numbers, \tilde{h} must map each curve α_k to β_k or its inverse; and since \tilde{h} preserves space orientation, we must have $\text{Lk}(\tilde{h}(\alpha_k), \tilde{h}(\alpha_j)) = \text{Lk}(\alpha_k, \alpha_j)$, $k, j = 1, 2, 3$. But, as just noted, the β_k cannot be oriented so that all three linking numbers are the same as for the corresponding α_k .

COROLLARY II.2. *There exists no isotopy of S^3 taking the graph M_n to its mirror image M_n^* ($n \geq 4$).*

Proof. We argue by induction on n , with the case $n = 3$ (Theorem II.1) as the start. Suppose $h: S^3 \rightarrow S^3$ is an orientation preserving space homeomorphism taking M_n to M_n^* . By Lemma II.2.1, h maps the cycle $a_1 a_2 \dots a_n a_1' \dots a_n' a_1$ to some cyclic permutation of $b_1 \dots b_n b_1'$ or its inverse. As in the proof of Theorem II.1, by following h with an isotopy if necessary, we may assume that h respects vertex numbering. But then, ignoring the edges $a_n a_n'$ and $b_n b_n'$ gives an orientation preserving homeomorphism of S^3 taking M_{n-1} to M_{n-1}^* (and respecting vertex numbering).

LEMMA II.2.1. *Each automorphism of the graph M_n ($n \geq 4$) leaves the cycle $C = a_1 a_2 \dots a_n a_1' \dots a_n' a_1$ setwise invariant.*

Proof. Since each vertex of M_n has order 3, any simple closed curve H containing (in order) vertices v_1, \dots, v_m determines a sequence e_1, \dots, e_m (possibly with repetitions) of

Fig. 6. Branched covers of M_3 and M_3^* .

edges of (the closure of) $M_n \setminus H$ where e_k is the unique edge of $M_n \setminus H$ that has v_k as a vertex. The cycle C contains all the vertices of M_n and has the additional property that if v_1, \dots, v_p are any p consecutive vertices, $p \leq n$, then no two of the edges e_1, \dots, e_p are the same. We claim that C is (up to cyclic permutation and reversing orientation) the only cycle in M_n having both of these properties. From this it will follow immediately that C is invariant under automorphisms.

It is convenient to introduce the following terminology: edges of M_n comprising C are called boundary edges; the other edges, of type $a_k a_k'$, are called spanning edges. The vertices a_k and a_k' are called duals of each other; the dual of any vertex v is denoted v' , with the convention that $a_k'' = a_k$. The dual of an edge (or union of edges) A is the edge (or union) determined by the duals of the vertices of A , and is denoted A' .

Now suppose H is a cycle $v_1 \dots v_{2n} v_1$ containing all the $2n$ vertices of M_n . By considering the set $H \cap C$, we shall show that unless $H = C$, H must contain short sequences of vertices that determine sequences of edges with repetition.

Assume $H \cap C$ is a proper subset of C . First note that since H, C contain all the vertices, and each vertex has order 2 in H and in C , it follows that for each vertex v of M_n , $H \cap C$ contains at least one of the edges of C incident to v ; in particular, each component of $H \cap C$ is an arc. We now consider the two ways that our claim that $H \cap C = C$ can fail: (1) $H \cap C$ consists of n pairwise disjoint edges, and (2) some component of $H \cap C$ is an arc consisting of two or more edges.

In case (1), we first observe that n must be odd since if n were even then H would contain a closed curve consisting of two dual boundary edges and the spanning edges connecting them. Assuming n is odd, let v_1, v_2, v_3, v_4 be consecutive vertices of C such that the edges $v_1 v_2$ and $v_2 v_3$ are components of $H \cap C$. Then the spanning edges $v_2 v_2'$ and $v_3 v_3'$ are in H . But since n is odd, the boundary edge $v_2' v_3'$ also is in H and so v_2, v_2', v_3', v_3 is a sequence of $\leq n$ (since $n \geq 4$) vertices of H for which two of the associated edges of $M_n \setminus H$ coincide.

In case (2), let A be a component of $H \cap C$ consisting of two or more edges; $A = v_1 \dots v_m$ for some $3 \leq m \leq 2n$. Then H contains the spanning edges $v_1 v_1'$ and $v_m v_m'$ but none of the spanning edges incident to v_k , $2 \leq k \leq m-1$. Thus either H contains no points of the open arc A' dual to A , in which case there would be no way for H to reach the vertex v_2' , or else we must have $H = A \cup v_m v_m' \cup A' \cup v_1 v_1'$. But then there is a sequence of four ($\leq n$) consecutive vertices v_2, v_1, v_1', v_2' of H for which the first and last are incident to the same edge of $M_n \setminus H$.

§III. CHIRALITY OF A MOLECULAR K_5

The graph M_3 discussed in Section II is homeomorphic to the bipartite graph $K_{3,3}$ which is one of the two basic nonplanar graphs of Kuratowski. The other, K_5 (complete graph on 5 points) also has been realized chemically. The molecule whose graph is shown in Fig. 7 was [8] synthesized independently in 1981 by H. Simmons *et al.* and L. A. Paquette *et al.* In Fig. 7, all but three of the vertices represent carbon nuclei, while the three marked "O" are oxygen, and,

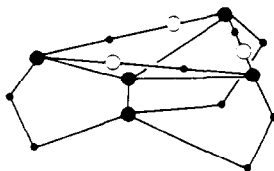


Fig. 7. Simmons-Paquette K_5 molecule.

as usual, the hydrogen nuclei that complete the molecule are suppressed. We thus have, as noted in [9], that the molecular graph is homeomorphic to K_5 with the additional data that there are three chemically different kinds of edges $C-C-C-C$, $C-C$, and $C-C-O-C$. As Walba noted elsewhere, it is convenient to abstract these differences as three colors, say green, blue, and red respectively and observe that the red edges are directed while the others are not. It is conjectured in [8] and [9] that the Simmons–Paquette K_5 molecule is topologically chiral; the methods of Section II provide the desired proof.

THEOREM III.1. *There exists no orientation preserving homeomorphism of S^3 taking the graph K_5 of Fig. 7 to its mirror image K_5^* respecting the three types of edges.*

Proof. In Fig. 8 the vertices of K_5 and K_5^* are labelled so that the edges 12, 23, 31 are “red” and directed, the edges $a1, a2, a3, ax$ are “blue” and the edges $1x, 2x, 3x$ are “green”; the edges of K_5^* have corresponding colors.

Suppose there exists an orientation preserving homeomorphism $h: S^3, K_5 \rightarrow S^3, K_5^*$. Because each type of edge must be sent to an edge of its own color, we must have $h(a) = a^*$ and $h(x) = x^*$. As in Section II, we can follow h with an isotopy if necessary (rotate about the vertical “blue” edge) so as to have $h(1) = 1^*$. Since h maps the oriented edge 12 to the red edge emanating from $h(1) = 1^*$, it must be the case that $h(2) = 2^*$ and, consequently, that $h(3) = 3^*$. In summary, we may assume that h respects the vertex numbering in Fig. 8.

Let C be the cycle $123xa1$ and $C^* = 1^*2^*3^*x^*a^*1^*$. As in the proof of Theorem II.1, since $h(C) = C^*$ and these curves are unknotted, we know that the 2-fold cyclic branched covers of S^3 branched along C and C^* are again S^3 and that h induces an orientation preserving homeomorphism $\tilde{h}: S^3 \rightarrow S^3$ mapping the lift of K_5 to the lift of K_5^* . Each of the five edges comprising $K_5 \setminus C$ (resp. $K_5^* \setminus C^*$) lifts to a simple closed curve and we shall see that the linking patterns of these two systems of curves precludes the existence of \tilde{h} .

In Fig. 9 we see the lifts of K_5 and K_5^* . Because h , hence \tilde{h} , respects vertex labels, \tilde{h} must map the cycles $\alpha, \beta, \gamma, \delta, \epsilon$ to $\alpha^*, \beta^*, \gamma^*, \delta^*, \epsilon^*$ respectively and the only question is whether we can choose compatible orientations of the various curves. Choose either orientation of α and then orient β, γ so their linking numbers with α are each $+1$. Then orient δ and ϵ so that $\text{Lk}(\delta, \gamma) = \text{Lk}(\beta, \epsilon) = +1$. With these orientations, $\text{Lk}(\delta, \epsilon) = -1$. On the other hand, if we

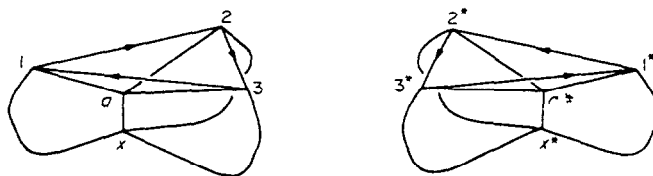


Fig. 8. K_5 vs. K_5^* .

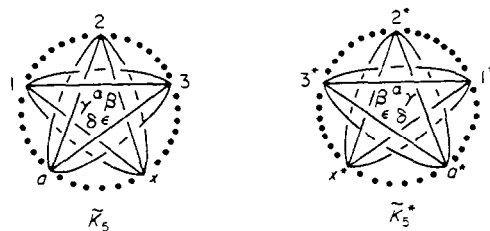


Fig. 9. Branched covers of K_5 and K_5^* .

apply the same rules to α^* , β^* , etc. we find that $Lk(\delta^*, \epsilon^*) = +1$. Thus the alleged \bar{h} cannot exist.

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REFERENCES

Note: Articles [1], [5], [7], [11] are fascinating and easy to read, with [11] the best start for a general introduction to stereochemical topology. Articles [8], [9] are more clearly aimed at chemists but are expository and readable; one should read [8] and then tackle [9] which is a definitive survey. The book [4] is a good source for the basic ideas and terminology of traditional stereochemistry.

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